UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/643,679	08/18/2003	Xavier Paliard	PP01612.009 (2300-1612.10	4593

27476 7590 01/24/2008

NOVARTIS VACCINES AND DIAGNOSTICS INC.
INTELLECTUAL PROPERTY R338
P.O. BOX 8097
Emeryville, CA 94662-8097

EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
01/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/643,679	PALIARD ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-5,8,23-40,42,45 and 46* is/are pending in the application.

4a) Of the above claim(s) *23-40 and 42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-5,8,45 and 46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/29/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

This is a response to the amendment filed on Oct. 29, 2007. Claims 3, 45, 46 have been amended. Claims 1-2, 6-7, 9-22, 34-36, 41, 43-44 have been canceled. Claims 3-5, 8, 23-40, 42, 45-46 are pending before the examiner. Claims 23-33, 37-40, 42 were withdrawn from consideration. Claims 3-5, 8, 45-46 are considered before the examiner.

Information Disclosure Statement

The information disclosure statement submitted on Oct, 29, 2007 (IDS) is in compliance with the previsions of 37 CFR 1.97. Accordingly, the IDS has been considered by the examiner.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Regarding the rejection of claim 5 under 35 U.S.C. 102(b) as being anticipated by Houghton et al. (1) (WO 91/15771A1) or under 102(e) as being anticipated by Houghton et al. (2) (US patent No. 5, 683,864A), Applicants submit that none of the references teaches the composition comprising an adjuvant. Applicants' argument has been fully considered; it is found persuasive. The rejection has been removed.

Double Patenting

3. The double patenting issue of claim 5 over claim 45 of Application No. 10,612,884 has been withdrawn because Application 10,612,884 has been abandoned.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 5 and 8 are still rejected under 35 U.S.C. 103(a) as being unpatentable over Cho et al. (Vaccine 1999, Vol. 17, pp. 1136-1144) and Lagging et al. (J. Virol. 1995, Vol. 69, No. 9, pp. 5859-5863) or Geissler et al. (J. Immunol. 1997, Vol. 159, pp. 5107-5113) on the same ground stated in the previous office action.

6. Applicants traverse the rejection and provide that according to the decision by the supreme court in KSR *Int' lco.v. Teleflex, Inc.* No. 01-1350 (US Apr. 03, 2007), the four factual factors in *Granham v. John Deerre,* 148 USPQ 459, 467 (US 1966) are still required. In particular, the supreme court in *KSR* still recognized that the prior art references must teach or suggest all the claimed limitations. Additionally, there must be a reasonable expectation of success. Applicants allege that based on the forgoing, the office has failed to establish a prima facie case of obviousness. In particular, both the primary reference by Cho and secondary reference by Lagging or Geissler et al. pertain to DNA immunization, not to the polypeptide immunization. Therefore, they are irrelevant to the claimed invention.

7. Applicants' argument has been respectfully considered; however, it is not found persuasive. Because while Cho and Lagging or Geissler only teach to use the polynucleotide encoding the fusion protein of HCV NS345 or core rather than the polypeptide directly for immunizing a subject to produce a significant immune response, it is well known for any one of ordinary skill in the art that the mechanism for a DNA vaccine being capable of inducing an immune response, the polypeptide encoded by the polynucleotide must be immunogenic. Since the immune response induced by the DNA vaccine is still based on the immune response against the polypeptide after the polynucleotide contained in the DNA vaccine is translated into the polypeptide antigen.

8. Applicants are reminded that The case law about *KSR International Co. v. Teleflex Inc.*– conclude that Ordinary Innovation is obvious. In *KSR*, the Supreme Court did not entirely reject the "teaching, suggestion, or motivation" test, but rather criticized the formalistic and rigid application of this test by the Federal Circuit in this case. The Court acknowledged that a patent composed of several elements is not proved obvious merely by demonstrating that each of its

elements was independently known in the prior art. **But, the Court ruled that any teaching, suggestion or motivation does not need to be explicit and courts can take into account the inferences and creative steps that a person of ordinary skill in the art may employ: "A person of ordinary skill is also *a* person *of ordinary creativity*, not an automaton."** In order to determine whether there was a reason for one skilled in the art to combine known elements in a manner claimed by the patent, courts must analyze the interrelated teachings of prior art references, the effects of known demands in the marketplace, and the background knowledge possessed by a person of ordinary skill in the art. The Supreme Court stated that the combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results, and further indicated that any of the following may provide a "reason" for combining these known elements: a need or problem known in the field of endeavor at the time of invention and addressed by the patent; an obvious use of familiar elements beyond their primary purposes; or a design need or market pressure to solve a problem (Morrow et al. The case law about *KSR International Co. v. Teleflex Inc.* – conclude that **Ordinary Innovation** is **obvious**.

9. In the instance, when the polynucleotide encoding the HCV NS35ab and core are proved to be immunogenic, a suggestion or motivation for using the polypeptide encoded by said polynucleotide as an antigen directly does not need to be explicitly disclosed by the prior art, the courts can take into account the inferences and creative steps that a person of ordinary skill in the art may employ. "A person of ordinary skill is also *a* person *of ordinary creativity*, not an automaton." Furthermore, the combination of familiar elements of HCV nonstructural proteins and core protein antigens as well as combination of an HCV antigen with an adjuvant according to known methods is also likely to be obvious when it does no more than yield predictable results.

10. Hence, absence of an unexpected result to the contrary, the claimed invention as a whole is prima facie obvious absence unexpected results.

11. New ground of rejection:

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

13. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claims 3-5, , 8, 45 and 46 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 3, 4, 10, 13, 20, 21, 22, 23 and 75 of copending Application No. 10,281,341. Although the conflicting claims are not identical, they are not patentably distinct from each other because the conflict claims in the co-pending application is the species of the generic claims of the current Application, which comprises all limitations of the current claims. Particularly, the claims of the current Application use open language "comprising" to describe the claimed composition, which fails to define the claimed composition not containing other ingredient such as the polynucleotide encoding the

E1/E2 polypeptide cited in the conflict claims. To this context, the conflict claims in the copending Application can be interpreted as a species of the generically claimed compositions in the claims of the current Application, which anticipate the claims 3-5, , 8, 45 and 46 of the current Application.

15. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. Claims 3-5, 8, 45 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liao (WO 96/38474A2), Beld et al. (Hepatology 1999, pp. 1288-1298) and Valenzeula et al. (WO 97/44469A2).

18. The claimed invention is directed to an immunogenic composition comprising a fusion protein encoding the polyprotein of HCV core, and NS345ab and an adjuvant with a pharmaceutical acceptable excipient, wherein each or HCV polypeptide can be from a different strain of HCV.

19. Liao et all describe an immunogenic composition comprising HCV core polypeptide combined with a non-structural protein particularly the HCV NS5 and NS3-4 nonstructural proteins (See page 18, especially lines 10-15). Liao et al. also teach that adjuvant can be used for increase the resultant immune response generated by said immunogenic protein in the composition (page 26, paragraph 1). Liao et al do not explicitly teach if the combined use of the HCV core antigen with the non-structural protein NS34 and NS5 is constructed as fusion protein. Liao et al. do not teach that one of the HCV polypeptides or each of the HCV polypeptide is from different strain of HCV than the other HCV polypeptides.

20. However, it is well known for any one with ordinary skilled in the art that HCV is a RNA virus with many genotypes, wherein the variations or mutation unexpectedly occur in many locations spreading in core, NS3 , NS4 and NS5 regions as evidenced by Beld et al. (See entier document, especially Fig. 3). In order to produce an immune response for many different genotypes of HCV with one antigen polypeptide, Valenzeula et al. teach a method using a fusion polypeptide that expresses multiple epitopes of different structural and non-structural proteins from different genotypes of HCV strains, which is referred as a Multiple Epitope Fusion Antigen (MEFA). For example, a MEFA fusion protein can comprise a core antigen from HCV genotype 1 and at least one NS4 antigen from HCV genotype 2 and/or 3 (See pages 14-18).

21. Therefore, obviously to make such an immunogenic composition capable of induce a significant immune response against more than one genotypes of HCV, one of ordinary skill in the art at the time of the invention was filled would have been motivated by the cited references to construct an antigenic fusion protein comprising as much as possible antigen epitopes of HCV core, NS345ab that must have been derived from different genotypes or strains of HCV, and preferably in the presence of an adjuvant.

22. As there are no unexpected results have been provided, hence the claimed invention as a whole is prima facie obvious absence unexpected results.

Conclusion

23. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 6:30 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Baoqun Li

Bao Qun Li

BAOQUN LI, MD
PATENT EXAMINER